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PRIMARY CARCINOMA OF THE URETERS.

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IN April, 1905, a case came under observation at the Surgical Clinic of Greifswald, which is of great clinical interest on account of the peculiarity of the symptoms presented, as well as the pathologic findings. A female, sixty years of age, gave the following history: At about the age of five or six, she had scarlet fever and measles. Married at seventeen, she did not become pregnant. Her husband died five years after marriage from pneumonia. At the age of twenty-seven years she married for the second time, going through two normal pregnancies, but after the first pregnancy she suffered from jaundice for about five or six years. During this time, in the summer months, she frequently complained of abdominal pain after hard work, but this, however, soon passed off and she did not feel ill in any other way. Since last summer she has again complained of constant pain in the abdomen. At the end of November, 1904, she fell, striking on the right side, since which time she has had constant pain, located in the back and extending towards the right side. At the end of March, 1905, her physician diagnosticated a right-sided nephroptosis; at the same time a tumor appeared in the right side of the abdomen, and as the latter increased in size and the pains increased, the patient came to the clinic.

She was a middle-sized, strongly-built woman, with well-developed muscles and considerable fat. The circumference of

the abdomen was 99 cm., the abdomen being much distended, the right half protruding more than the left. On the right side of the abdomen resistance was felt by palpation and by careful examination a tumor the size of a child's head was discovered, having an irregular surface. It occupied almost the entire right side of the abdomen from the costal border to the anterior superior iliac spine, causing some protrusion of the inguinal region. It extended somewhat towards the liver, did not move with respiration and did not continue into the small pelvis by a pedicle. Some amount of tenderness on pressure could be elicited in the upper part of the tumor under the right costal margin and the growth appeared to be slightly movable. On the left side of the abdomen, between the umbilicus and the iliac spine, some tenderness was produced on deep palpation and here a sensation of varying resistance could be made out.

The kidneys could not be palpated, as they were in their normal position and the abdominal wall was very thick.

Examination of the urine gave the following data: It was passed spontaneously in small quantities, being cloudy and slightly acid in reaction. Upon filtration, it was found to contain albumin, but no sugar. By centrifugation a good amount of flaky sediment was obtained, which contained numerous granular casts, flat epithelial cells, representing those coming from the vesical mucosa, and also a few red and white blood corpuscles.

The lungs were normal. The first sound over the cardiac apex was not clear, while the second aortic was accentuated.

On the left side of the forehead, over the frontal sinus, existed an exostosis the size of a hazelnut, having a smooth surface.

Both legs presented varicose veins, particularly marked on the right. These, however, gave rise to no symptoms.

Nothing of importance was found by vaginal examination. No connection could be detected between the tumor and the genital organs. Rectal examination negative.

Upon insufflation of the colon, it was found that the latter covered the tumor in front, also between the growth and the liver.

Cystoscopy gave the following results. The bladder was small, being only able to contain a little quantity of urine, hardly amounting to 100 cc., and could only hold the irrigation fluid for

a short time. The vesical mucosa was pale and the region of the ureters protruded. The left ureteral orifice projects markedly and from this urine occasionally bubbles out, which did not seem to be cloudy. In place of the right ureteral orifice a conical shaped growth, almost as large as a cherry, and having a smooth surface was seen and here no ureteral orifice could be distinguished. The tumor was evidently greatly prolapsed and edematous ureteral mucosa. The mucous membrane of the bladder in the neighborhood was also swollen and edematous. At no point, however, was there any marked vascular injection. The right ureter cannot be catheterized, but the left could, the instrument being pushed 25 cm. upward to the pelvis of the kidney. In three-quarters of an hour 28 cc. of slightly cloudy, dark yellow urine was obtained and during all this time not a single drop came from the right ureter. No calculous formation could be found in the protrusion of the right ureter.

Cryoscopic examination of the urine obtained from the left kidney showed a decrease in the freezing point, it being 0.98° .

On the day before the operation the patient constantly complained of pain in the right side of the abdomen, which at times was so severe that she was obliged to leave her bed, walk around, or sit, with the body bent over. The amount of urine voided in twenty-four hours varied between 400 and 520 cc.

A diagnosis of right-sided hydronephrosis, from obstruction of the right ureter, was made, the obstruction being thought to exist at the lower part of the latter and either resulting from a calculus lodged in the duct, a cicatricial stenosis or a neoplasm.

Six days after the patient's admission to the hospital, operation was undertaken. A long incision was made on the right side of the abdomen from the twelfth rib to the anterior superior iliac crest. The free extremity of the twelfth rib was resected to the extent of about 4 cm. in order to give more space. After the soft structures and the fatty capsule had been dissected off, a renal sac, quite as large as a child's head was brought forward, it being quite firmly adherent to the liver at its upper pole. Puncture of the sac gave exit to $1\frac{1}{2}$ litres of a blackish brown fluid, holding in suspension numerous fibrin flakes. The renal sac, which consisted of two compartments, was then opened. The interior of these sacs was lined with numerous layers of fibrin. Little of the

renal parenchyma remained. The ureter was greatly dilated and at its lower part there existed a hard neoplastic thickening. Since this kidney had lost all its functions it was removed and upon separating the upper pole from the liver the peritoneum was torn at two points and at the same time a hard, circumscribed growth was removed, which occupied the upper renal pole. Upon cross section it was found that there were metastases in the liver and in the centre of a nodule, which was the size of a walnut, softening had occurred.

The ureter was completely removed and ligated at its lower end. Its lumen contained thick pus, while the neoplastic-like thickening at the lower end could not be reached through the incision, so that resection of this portion had to be postponed to a second operation, because the patient began to give evidence of weakening, and the operation had to be completed at once. Two strips of iodoform gauze were pushed down to the stump of the ureter and after the pedicle of the kidney had been tied off two clamps had to remain upon the stump. Apron tampons were pushed in over the wound in the liver and iodoform gauze was used as packing. At the end of the operation a litre of salt solution was given subcutaneously.

The patient returned to consciousness soon after the operation and did not complain of much pain, but about eight hours later sudden collapse occurred and she died with symptoms of embolus.

Autopsy. Medium size, strongly built, fat cadaver, of an elderly woman, abdomen somewhat pendulous; a large and perfectly fresh operative wound extending in the right lumbar region along the border of the ribs. Abdominal cavity opened. The omentum possessing much fat dips down in the pelvis. Its surface, as well as that of the intestinal coils lying underneath and parietal peritoneum is covered with a thin layer of fluid blood, several cubic centimetres of which had collected on the surface of the pelvic organs. On the right, underneath the liver, as well as on the mesocolon of the ascending colon, is covered by gauze filling up the abdominal space. The lower portion of the small gut was first separated from the ascending colon and caecum so that the large operative cavity was exposed. This was bounded above by the lower border of the right lobe of the liver; extending along the spine it passed near the inferior vena cava, while below it

reached the entrance of the pelvis. It was perfectly dry everywhere, containing neither blood nor pus, while no reaction in the tissues could be found.

The left ureter was then exposed, to the extent of 5 or 6 centimeters and was found normal in color and nowhere dilated. The left kidney and supra-renal capsule were in normal position. The left kidney was of medium size, measuring 13 cm. in length, 5 cm. in width and 3 1-3 cm. in thickness, so that it did not appear as if it alone performed the functions of both organs for any length of time. Its capsule was easily stripped and its surface was then found to be pale red, containing a surprisingly small amount of blood, but nowhere could any cloudiness be detected. The medullary substance was also light red and transparent, while the straight urinary tubules showed themselves in the form of distinct, delicate light grayish red stripes, reaching the points of the papillae. Fresh microscopic section showed a transparent condition of the convoluted urinary canals, while in the straight urinary tubules of the medullary substance were many casts and much blood pigment in the epithelium. The calices and renal pelvis were lined with a white mucous membrane.

The right kidney was absent, as well as a large portion of the upper part of the ureter. In order to examine the remainder of the tube, the bladder was opened in the median line, giving exit to some clear colorless urine. The vesical mucous membrane was very white and only in the region of the urethral orifice was there some slight vascular injection. The orifice of the left ureter appeared as a small opening on a level with the bladder wall, whereas, on the right a projection was seen, the size of a small hazelnut, very soft in consistency and through the centre of which a fine probe could be passed into the right ureter, the latter containing from ten to twelve cc. of urine, which made its exit when the instrument was pushed through the stump in the operative wound.

The soft medullary growth showed upon fresh microscopic sections an epithelium containing large oval nuclei and distinct nucleoli and represented large flat laminated epithelium, rich in protoplasm, and often supplied with pointed cell processes, among which transitional forms of cylinder cells could be distinguished.

On attempting to reach the bladder from above, through

the ureter, firm occlusions were met with which at first appeared to be of a calculous nature, but upon section, they were found to be thickened portions of the walls of the ureter in the form of small projections the size of a pea, around which existed a thick layer of cicatricial tissue. Extending about four to five cm. upward from the bladder the same milk-white neoplastic masses were found over the inner surface of the ureter, similar to the soft nodule appearing at the ureteral orifice and penetrating into cavity of the bladder. At a point about 12 cm. from the bladder and where a calculous had been suspected to exist, a thick hard substance similar in structure to a scirrhus could be traced up from the ureter into the fatty tissue.

The uterus contained several myomata the size of a walnut and many of these had become hardened, while others showed a firm, fascicular grayish white aspect on section. The vaginal walls were perfectly normal. A few mucous and small Naboth's glands projected in the portio vaginalis. The uterine mucosa was of a delicate grayish red. Rectum intact, its mucous membrane grayish red.

The right iliac vein, like all that portion of the inferior vena cava up to the liver was obstructed by hard, dark red and loose thrombi which, from their external aspect contained distinct whitish spiral lines.

The liver was 28 cm. in width, 21 cm. in height and $5\frac{1}{2}$ cm. in thickness. The gall bladder, which was almost completely filled with small sharp calculi rested upon the free border of the liver on the right in the neighborhood of the operative wound. The surface of the right lobe of the liver was adherent to the surrounding structures by many firm, fibrous adhesions. At this point near the wound was an irregular and quite deep laceration, $10\frac{1}{2}$ cm. in length and $3\frac{1}{2}$ cm. in width, filled with clotted blood. 6 cm. above at a point where the border of the liver came in contact with the diaphragm was found a flat, white carcinomatous nodule, its length being $4\frac{1}{2}$ cm., its center containing a marked depression, while it protruded above the surrounding structures to the extent of 1 cm. Upon cross sections of the liver carcinomatous nodules were found at many places, varying in size from a hazelnut to a pigeon's egg; they were bright red in color, of soft consistency, so that any line of demarcation from the hepatic

parenchyma was quite indistinct. There was also some yellow discoloration of the hepatic parenchyma. The left lobe extended unusually high up and like the right was adherent at several points. Six cm. to the right of the gall bladder was found a spot of hemorrhagic infiltration on the free border of the organ, where apparently, during the operation adherent fatty tissue had been dissected off and at this point a grayish red carcinomatous nodule, about the size of a cherry, was found, quite sharply defined from the surrounding parenchyma.

The spleen measured 11 cm. in length, $9\frac{1}{2}$ cm. in width and $3\frac{1}{2}$ cm. in thickness. It was everywhere dark red, of firm consistency and smooth on section.

The heart from base to apex measured 11 cm. the width of the aortic valve was $7\frac{1}{2}$ cm.; muscular tissue at the base 2 cm. in thickness, in the middle $1\frac{1}{2}$ cm. and at the apex 1 cm. Right ventricle; width of pulmonary valve $7\frac{1}{2}$ cm.; thickness of muscular tissue averaged about 5 mm.

The right lung contained on its posterior border about midway between the apex and the base, a soft grayish white carcinomatous nodule about the size of a walnut, otherwise both lungs were filled with air, hemorrhagic and somewhat edematous.

Section of the brain showed slight hemorrhage, otherwise no marked changes.

Around the abdominal aorta in the region of the lumbar vertebrae the tissues were of firm consistency so that when separating the vessel from the vertebral column no loose connective tissue could be found. Section through the lymphnodes and surrounding fat showed that the structures had been transformed into carcinomatous substance, gray in color and of the same nature as that described in the middle portion of the right ureter.

Anatomical diagnosis: Carcinoma medullare ostii dextri, carcinoma scirrhosum partis mediae ureteris dextri. Infiltratio carcinosa telae adiposae retroperitonealis lateris dextri et glandularum retroperitonealium regionis lumbalis. Carcinomata medullaria metastatica hepatis et metastasis pulmonis dextri. Ren dexter operatione remotus. Hypertrophia renis sinistri dubia, nephritis medullaris. Anaemia cerebri. Adipositas cordis, obesitas universalis.

Microscopical examination. Stained sections of the ureteral

neoplasm and hepatic metastases gave the following results. The sections included the ureteral neoplasm from the soft medullary portion to the hard scirrhous parts. It was then found that the medullary growth was composed of carcinomatous cells presenting great variety. They were closely crowded together so that no alveolar structure could be recognized. At several points cell masses could be distinguished from the surrounding cell elements in that at these points the cells had lost their shape, structure and staining properties, so that they could only be indistinctly made out, showing that death had taken place. These necrotic portions were surrounded by rapidly growing cell elements. The carcinomatous cells were of the large protoplasmic, epithelial type, with thick, oval nuclei. Their shape demonstrated beyond a doubt that they originated from the epithelium of the ureter. Just as is found in the epithelium of the ureter, so among the neoplastic cells, all varieties of transitional forms were found, from the flat cells with pointed offshoots, frequently resembling a tail, to the cubic, polymorphous and cylindrical cells. The nucleoli and the substance of the nucleus were very marked in the nuclei and at some portions of the section cell division was taking place.

Starting from the medullary substance a tissue zone was found where extension of the carcinoma was effected into the neighboring structures and here, instead of the large cell clusters, small ones are seen, separated from each other by narrow bands of tissue. Here the carcinomatous cells have apparently penetrated into the lymphatics and have filled them up by active cell growth. Therefore, according to whether section of the lymph space was made longitudinally or transversely, one sees carcinomatous nests or plugs. Further off, where the growth had not reached this development, alveoli and tube-like formations were met with. The nearer one reached the periphery of the growth, the smaller became the cell clusters and the larger the tissue spaces, until at last at certain isolated spots, a small number of carcinomatous cells were seen lying in circles or in rows.

It is of special importance to remark that similar formations of cancrioid pearls occur distributed throughout the growth and which were very clearly demonstrated in sections stained by van Gieson's method. The borders of these formations had large

cubic cells possessing a distinct nucleus, while in the more central portions, flatter cell types existed, lying in concentric layers, while in the very center horny cells without a nucleus were present and which took a deep yellow stain.

The structure of the stroma of the growth was not uniform, and varied according to the extension of the neoplasm in the different zones.

In the immediate neighborhood of the centrally located medullary carcinoma foci, the tissue strands were very narrow, representing the transition between these and the larger clusters of carcinomatous cells. Further beyond, the clusters were separated from each other by loose, soft tissue. At this point many tissue cells were piled up in a loose network, which became wavy. In the periphery, however, which only contained isolated clusters of tumor cells, the character of the stroma was represented by firm fibrous tissue, while thick and wavy layers of tissue lay parallel and close together, including only a few isolated tissue cells. This part of the section represented the hard nodule which clinically was supposed to be a calculus lodged in the urethra, when the urethral catheter was passed.

As so frequently occurs in the development of carcinomata, there was in the case just reported some intermediate tissue where it borders on the rapidly growing neoplastic cells, during inflammatory reaction. The stroma was infiltrated with round cells, which were found wherever carcinomatous cells occurred, because they participated in the extension of the neoplasm.

From the macroscopic findings one might easily come to the conclusion that besides the medullary growth existing at the ureteral orifice, another type of cancer, namely scirrhus, had developed at some distance from and independently of the former. However, microscopically it was distinctly shown that both types of cancer were not sharply defined from each other and that a gradual transition from one type to the other occurred. The development of the scirrhus can be explained by the peculiar reaction of the tissue to advancing carcinomatous cells, becoming converted into firm, cicatricial tissue. The cells of the scirrhous portions were without any doubt derived from the medullary carcinoma.

This opinion is strongly supported by the microscopic findings in the metastases in the liver. They very closely resembled the primary growth, inasmuch as the structure of the new growth possessed no uniform character and here also all the transitional forms from medullary carcinoma to scirrhous were to be found. The cells perfectly resemble those of the primary growth, both in shape, arrangement and distribution. The formations resembling cancrioid pearls also occurred. The stroma in the metastases was very marked. The development of this stroma can be explained from the fact that from the neoplastic cells a marked reactive overgrowth had taken place in the scant, but normal hepatic interstitial tissue, which, for the most part, had been converted into cicatricial tissue.

The case here reported is without doubt extremely rare. The ureter is certainly far less apt to give rise to primary tumors than the bladder or renal pelvis. When a primary ureteral growth occurs, it is generally in the form of a nodular tumor and it certainly rarely happens that these growths arise in the ureter and belong exclusively to it. As a rule malignant neoplasms originate in the renal pelvis and from this point extend down into the ureter. Under the head of nodular tumors of the ureter, benign fibromata are to be classed on the one hand, while sarcomata and carcinomata on the other. It often also happens that a papillary growth will be found of a carcinomatous nature upon section, while at another part it may still retain a benign character.

Von Lichtenheim was only able to collect a few instances of alveolar sarcoma, von Willutzki one instance of sarcoma of the upper portion of the ureter and von Ribbert one instance of poly-pous myosarcoma.

Nodular growths of the ureter are of more frequent occurrence. Israel mentions two instances; the first case was a growth the size of a cherry, arising from the mucosa of a dilated renal pelvis, the neoplasm consisting of papillae, closely crowded together and extended a little into the ureter. In the second case the renal pelvis was dilated to the size of a walnut and upon cross section the mucosa was found covered with nodular growths closely crowded together. Directly continuous with this was a nodular growth, occupying the entire upper pole and a portion of

the middle third of the renal parenchyma. At many points the growth invaded the cortex so that a layer of renal parenchyma, varying from two to three millimetres in thickness, separated the neoplasm from the capsule. The mucosa of the dilated ureter was covered with many wartlike, pedunculated tumors, some being isolated, some collected in small clusters, while still others were arranged in a circular fashion around the entire circumference of the ureter, to such an extent that at a point 9 centimetres above the entrance of the ureter into the bladder, their development was so marked they must have caused obstruction. From this point downward the number and size again decreased so that only some small isolated papillary growths could be found on the vesical mucosa on the left. Microscopical examination in both cases showed that the growths were carcinomata, their cells having characteristics of transitional epithelium.

Busse has recorded two cases of malignant transformation of the entire urinary tract on one side. The first case represented numerous fibromata as well as benign nodular growths in the bladder, in the greatly distended ureter and in an enormously dilated renal pelvis. Twenty years previously the patient had noticed blood in the urine, this recurring at certain intervals. Pain in the right renal region caused him to come to the hospital and here a tumor was discovered. Operation showed that the kidney was also in a state of hydronephrosis, the renal pelvis being completely covered by papillary growths on its mucous membrane. Death occurred six weeks later from gangrene of the lung and at the autopsy nodular growths were also found in the lower end of the ureter as well as in the bladder.

The second case also occurred in a male, 55 years of age, who, for seven years had periodically passed blood in the urine and on account of the recent development of pain and pressure symptoms in the left renal region he entered the hospital. A large hydronephritic kidney, fully the size of an adult's head, was removed, as well as the surrounding tissue which had undergone purulent inflammatory changes. The mucosa of the renal pelvis was found covered with countless small warty growths, likewise the ureter. The patient lived five months after the operation, but continued to decline in health and finally died. At post-

mortem, a large infiltrating tumor was found in the walls of the bladder, while the ureter contained a large number of villous growths. Upon microscopic examination the tumors in the renal pelvis and ureter, likewise those in the bladder, were large-celled carcinomata.

Poll has described a case of multiple villous growths of the left ureter and renal pelvis. The entire mucosa of the renal pelvis was involved as well as the greater part of the ureter in the neighborhood of the kidney. The histological structure of the ureteral and renal pelvis growths was that of an ordinary papilloma, while on the other hand, the neoplasm had begun to undergo a malignant transformation in the calices.

Kohlhardt has described a benign multiple villous growth in the renal pelvis and ureter.

Albarran's teachings relative to primary epithelial new growths of the renal pelvis and ureter are practically as follows: Most frequently they are papillomata, Albarran having collected eighteen instances. They usually develop upon the base of the renal pelvis and then continue downward toward the ureter; primary carcinoma of the ureter is extremely rare. Papillomata of the renal pelvis and ureter resemble those encountered in the bladder; they are usually multiple. This authority was only able to collect thirteen cases which were not papillary epitheliomata. The origin of these growths is quite the same as that of papillomata. Usually they are alveolar, more rarely cylindrical celled epitheliomata.

In those cases where the papillary new growth is confined to the ureter, and consequently without doubt primarily arise therein, are of far greater rarity and relative to this I would quote a case related by Neelsen. On the right side were two ureters entering the bladder 5 cm. in front of the neck. The upper part of the two ureters originated from the greatly dilated hydronephritic upper renal pelvis and showed marked pathologic change at its upper portion, while the lower two-thirds of the ureters were normal in size, with thin walls and pale mucous membrane; the upper third was enlarged and funnel-shaped for about the extent of 6 cm. and before being opened it felt soft and elastic. Upon section, it was found that this increased consis-

tency was due to the presence of numerous papillary growths placed closely together and arising from the ureteral mucosa which corresponded in appearance with the ordinary vesical papillomata. Some of them formed flat, broad vegetations, while others were larger, thin, pedunculated and coxcomb-like, lobulated or irregularly branched growths having a grayish red color and a soft consistency. The growths grew superficially. Microscopically they were found to be benign fibromata.

A benign villous growth originating in the left ureter has been described by Jebens. I would also refer to a case described by Hasenmyer of a villous tumor the size of an apple, which surrounded the right ureteral orifice. This case was also a benign papillary fibroma.

Jona has published a case of a primary ureteral neoplasm of an epithelial nature, but not papillary in construction. The growth which was about the size of a large hazelnut was situated in the lower portion of the left ureter near its entrance into the bladder. It was attached to the ureteral wall by a pedicle about 1 cm. in length and had developed toward the abdominal cavity pushing the peritoneum in front of it and was enclosed in the latter quite like an intraperitoneal organ. At the centre of the cross section of the growth was found an opening about as large as a pin's head which, on longitudinal section, was found to be a thin tube running through the tumor mass and ended as a diverticulum with which it was connected by a pedicle. This diverticulum from which the growth had originated, owing to its origin, must be considered analogous to a double ureter. This authority also makes the statement that fissuring of the ureter, or conditions similar to those met with in his case, seem to predispose the structures to neoplastic development just as in Neelsen's case, where the villous polypi had developed in a double ureter. In Jona's case, microscopical examination showed that it was not one of true adenoma, but an epithelioma having a cystic arrangement.

Ureteral neoplasms having a decided carcinomatous nature are of extreme rarity. The majority of carcinomata of the ureter which have been published, did not develop primarily in the ureter, but have spread to it from the neighboring organs, such as the intestines, genitalia and so forth, an example of which has

been described by von Litten, in which the stomach was the starting point of the malignant tumor, the left ureter becoming secondarily involved.

A second case of primary carcinoma of the ureter was recorded in 1896 by Rundel. The tumor which measured 4" by 2" in diameter was situated in the lower portion of the right ureter, which it surrounded. It was adherent to the base and posterior vesical wall and it invaded both seminal vesicles and vasa differentia. In consistency it was soft and of a whitish color. Above the growth the lumen of the ureter was dilated, especially at its middle third. Nodules were seen on the mucous membrane, isolated and in clusters to within one inch of the renal pelvis. A pea-sized polypus was found projecting through the ureteral orifice into the bladder and was composed of small, closely connected papillae. Metastases of the growth were found in the liver, lungs and abdominal lymphnodes. Microscopically the growth and metastases represented the flat epithelial carcinoma, with granular degeneration in the central cells. This growth occurred in a male 46 years of age who entered the hospital with symptoms of hydronephrosis. As cachexia was present the diseased kidney was not removed.

The case I have reported shows marked differences from all others so far recorded. The papillary construction of the tumor was wanting, likewise the usual multiple villous, or papillary formations on the vesical mucosa, renal pelvis and upper part of the ureter. In character our case corresponds rather more to a gastric carcinoma, in that it grew by continuity and gave rise to metastases in distant organs. It originated in the vicinity of the ureteral orifice, beginning as a medullary sarcoma and extended towards the bladder in the form of a projection the size of a hazelnut and towards the kidney completely obstructing the lumen of the ureter and then it took on more the character of a carcinoma, extending to the upper portions of the ureter and surrounding fatty tissue.

In closing I would like to refer to the connection between carcinoma of the urinary tract and calculous formation. As to primary carcinoma of the gall bladder and the large bile ducts, it is generally admitted that gall stones are the etiological factor of the malignant growth. Now, it is admitted that by continuous

pressure of the stone upon the mucosa an irritation is produced, which causes the development of carcinoma, or, at least, favors it, and this theory rests upon the fact that gall stones and carcinoma frequently coincide. The gall bladder itself gives rise to the formation of the calculi and retains them for a long time, while, on the other hand, certain portions of the bile ducts are often involved when large stones become imbedded and produce severe pressure irritation with repeated attacks of colic.

These portions are, in the first place, the pars duodenalis of the choledochus at the point where its lumen becomes narrowed, as well as the point of union between the cystic and hepatic ducts, where the lumen is also less.

Uliszewski has expressed himself as follows: "The question of the etiology of carcinoma of the biliary tract is at present not settled. That at first the action of the calculi is considered, is evident, firstly because the large majority of carcinomata of the gall bladder occur in cholelithiasis and beside because primary cancer of the bile passages gives rise to small strictures of about the same extent as a local inflammation resulting from impaction of a calculus might bring about. These cases represent about 40% of the entire number where calculi are suspected from the symptoms, or are actually found at operation or autopsy. In the case of the bile ducts we have the same reason to suppose that calculi are the cause, as in cases of malignant disease of the gall bladder. Generalization is not permissible, however, because Devic and Gallavarbin have quite properly called attention to the fact that stones and cancer of the gall bladder frequently occur in females as a result of lacing, whereas, as many men as women are affected with carcinoma of the bile ducts. Microscopical examination, also, fails to give any light on the matter. If the cases which were first examined here in the Pathological Institute where there was metaplasia of the epithelium of the gall bladder into sclerotic flat cells produced by gall stones (Diss. Ohloff), then we would have a convenient means of deciding whether a calculus in the bile ducts could be the cause of carcinoma. The few statements made known at the present time (Weber, Diss. Würzburg) of this condition in the frequency of carcinoma of the gall bladder do not permit this conclusion."

The epithelial growths arising in the urinary tract including

the renal pelvis, ureter and bladder, have been mentioned as being produced by calculi. The chief reason for this is that upon several occasions vesical calculi have been found as well.

Wagner makes the following statement relative to this point. "Concerning the development of these tumors as little is known as about tumors in general; they usually occur between the ages of 40 and 60 years. The growths were found in males 24 times, 13 times in the female; 8 times calculi in the renal pelvis were observed." Those parts of the urinary tract above the bladder where stones are retained are the renal pelvis, the commencement of the ureter and its portion above the bladder where its lumen becomes narrowed. In those cases where primary growths are found at these points and in which calculi are present, it is very probable that the development of the tumor may be traced to pressure irritation from the concretion.

Such a case of renal epithelioma in which calculi were present has been reported by Shattock. He believes that the growth developed from the irritation of the calculi.

Le Dentu described a papilloma at the ureteral orifice complicated with a calculus: "After the kidney had been exposed by an incision the ureter was opened and a small calculus removed from it. Below this was a papilloma just allowing the passage of a sound past it, while a second similar growth was present near the bladder, completely obstructing the orifice."

Naturally, even these very important examples of the occurrence of tumors with stones are not proof of the development of the formation of the former from the latter. Even were it positive, one could not assume that every time that calculi are present, they are the cause of neoplasms in the renal pelvis and ureteral mucosa, because (1) the primary growths of the upper urinary tract rarely occur and in no way correspond with the frequency of calculus. This is especially true of the ureter. (2). Among the growths which have been observed, calculi have been present in only a few. (3). In our case, especially, the carcinoma developed at a spot in the ureter which certainly is very commonly the seat of impacted calculus, but no stones were found either during life or at the autopsy. (4). As to growths arising from the vesical mucosa, calculi cannot be held entirely respon-

sible, for the process can be traced back to the poisonous action of the various aniline dyes, because ulcer of the bladder is very frequently observed in employees of aniline factories (Rehn).

Therefore, we come to a conclusion similar to that reached by Uliszewski relative to the origin of primary carcinoma of the biliary tract and in closing I would say that the etiology of primary malignant tumors of the upper urinary passages is at present unknown like that of tumors in general.

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PROSTATIC ALBUMIN AND ALBUMOSE.

By EDGAR G. BALLENGER, M. D., Atlanta, Ga.

IN the New York *Medical Journal* for Feb. 24th, 1906, I called attention to the fact that the diseased prostate, like the diseased kidney, secretes albumin, and showed that this secretion might escape through the deep urethra into the bladder and be mistaken for that of renal origin.

So uniformly have I found proteid in the urine passed after massage of the inflamed prostate and so reliable has it been in the diagnosis of this condition that it is with pleasure that I comply with the request of the Editor of the *AMERICAN JOURNAL OF UROLOGY* to present further details of the subject.

Recently I have been making the test for albumin and albumose as a routine examination of the urine passed after massage, and have found it present in 25 patients with inflamed prostates and seminal vesicles. In no case was it found when the prostate and vesicles were normal, the test being negative in 15 patients with healthy prostates. One patient with marked hypertrophy, but no inflammation of the gland, failed to show albumin, although it was dense and hard and resulted in almost complete obstruction to the passage of urine. Two patients with acute prostatitis, for a few days had as much as one per cent. of proteid in the urine without any renal involvement. This could be greatly increased by massage of the prostate. Numerous tests were made upon all of the patients.

As a simple method of diagnosing prostatic inflammation I think it has no superior and that it may be depended upon with as much certainty as renal albumin in disease of the kidney, with this advantage, that it is less difficult to determine accurately the origin of proteid from the prostate than that from the kidney.

The test is available whether a microscope is at hand or not and requires no skill or experience to make a positive diagnosis immediately, even when there are scarcely any shreds and very little cloudiness in the urine passed after massage, which would ordinarily mean inflammation. In practical experience I have

often had a feeling of uncertainty as to whether or not certain prostates were chronically inflamed, without making a careful microscopic examination of the débris, for the absence of macroscopic shreds or masses in the urine after massage does not necessarily mean that the prostate is normal. In patients with an inflammation of mild character there appears to exist an interesting relation between the threads and the proteid; if the shreds are numerous the amount of proteid is small, but when there are no shreds there is much more albumin and albumose. The only explanation I can give for this is that the proteid material seems to be appropriated in some way in the coagulation of the threads. There are many patients with chronic prostatitis where the epithelial lining of the ducts and follicles is chiefly involved and where there are no nodules or enlargement of the gland perceptible, and yet there will be albumin present in the secretion and a chronic or recurrent urethritis kept up by it. A mistaken idea is prevalent both among the patients and the medical profession that a palpable defect must be present in all chronically inflamed prostates. In not a few patients a feeling of fullness or discomfort and a little difficulty in urinating will be the main symptoms, the gland feeling normal by rectal examination and the amount of débris, etc., massaged into the urine will be so slight that one hesitates to make a diagnosis of prostatitis without a microscopical examination. It is in these obscure cases with only a mild inflammation that the presence of albumose and albumin is of particular value in the diagnosis.

Until after repeated examinations of normal prostates I thought the albumose of the seminal fluid might be expressed from healthy vesicles and give an albuminous reaction, but practically it is very unusual after ordinary massage of the prostate and vesicles to get enough seminal secretion to respond to the ordinary tests for proteid. The amount present in normal semen is small. Consequently I believe that when the urine after massage contains a large amount of albumin or albumose, it invariably means disease of the prostate or seminal vesicles.

The amount present at each treatment also furnishes exact information as to the progress being made.

The patient should urinate in two glasses and be requested to retain a few ounces in the bladder after massage. If difficulty

is experienced in voiding the remainder an irrigation may be given and enough solution introduced into the bladder to enable the patient to urinate. More urine may be retained at the next examination, but it must always be remembered that if there is only a slight inflammation the proteid will be so diluted by a large quantity of urine or irrigating fluid that it may not be detected by the ordinary tests.

The quantity can be easily ascertained by boiling the urine in a test tube and precipitating the proteid with nitric or citric and picric acid. After standing, the amount thrown down multiplied by the total quantity of urine voided gives the amount of proteid given off by the prostate and vesicles. This in many patients will be equal in volume to the whole amount of urine passed after massage. ($\frac{1}{2}$ to 4 ounces). The mild cases may only show a trace. The amount varies with the degree of the inflammation and the frequency of massage.

If the precipitate is due to albumose it will clear up when heated to the boiling point. This form of proteid seems to be constantly present in the secretion from prostates and vesicles when they are chronically inflamed. (A small amount of albumose being present in normal semen). The heat test will usually be negative probably on account of the albumose which is not precipitated by boiling, and to the formation of an alkaline albuminate of the serum albumin, as the secretion is always alkaline in reaction. If the urine be added drop by drop to a test tube of boiling water the little white clouds will show the presence of proteid.

All other tests are positive, but the one which gives the best results and the one upon which I rely, is Robert's solution, as modified by Boston, containing 1 part of nitric acid to 10 parts of a saturated solution of magnesium sulphate. This does not cause the dark ring of oxidation at the junction of the fluids and for this reason is more delicate.

In explaining the presence of albumin and albumose in fluid from a diseased prostate, a study of the secretion which exudes upon the dressings of open lesions, throws some light on the subject. If the dressings from ulcers, boils, cancers, blisters, wounds, etc., be immersed for a short time in a half glass of water, and then filtered to free from any débris or pus, a large amount of

proteid will be present and responds to any of the usual tests. The amount from an abscess came as a distinct surprise to me when I first made this test. Abscesses of the prostate nearly always rupture into the deep urethra and often persist for many months draining through this canal into the bladder or as a discharge from the meatus. From a consideration of these facts it does not seem unnatural that we should not infrequently have urine-contaminated proteid from the prostate, without spermatozoa or anything to suggest its origin, unless these facts be born in mind.

The first urine washing out an inflamed urethra, when filtered contains more albumin than can be accounted for by the pus present, showing that inflammation of a mucous membrane will cause the exudation of a proteid material along with the leucocytes and not dependent upon them. It is the same kind of an inflammation that passes back into the prostate and vesicles where the secretion is retained and probably by tissue digestion or the influence of the alkaline secretion albumoses are formed. Pressure or overflow may force this fluid out through the deep urethra into the bladder. The smaller the amount of pus present the greater would be the danger of overlooking the source of the proteid and the more is the likelihood of an error being made in the prognosis and treatment.

A nidus of inflammation in the prostate gland or the seminal vesicle is one of the most important of the factors that tend to perpetrate a chronic urethritis. Much less skill is required to detect albumin in these secretions and to make a positive diagnosis than is necessary for a microscopical examination.

There is a striking resemblance between renal casts and urethral threads. Both are made of the coagulation of a material which exudes from an irritated or inflamed surface. They correspond accurately as to varieties: mucous shreds to hyaline casts, and desquamated epithelial threads to epithelial casts (which are granular if the cells have degenerated). Pus or blood may be incorporated in either shreds or casts. We know from a study of accessible lesions that proteid escapes from desquamated or irritated surfaces. Does this not suggest that perhaps there is a closer and simpler relation in certain cases between the secretion of albumin from the kidneys and that from other inflamed or eroded surfaces than we have realized?

Posner claims that 100,000 pus corpuscles in a cubic centimeter of urine corresponds to about 1 per cent. of proteid.¹ This may hold good where there is nothing but an inflammation; if, however, there is an abscess of the prostate or an ulcer of the bladder, it would be entirely misleading to depend upon this ratio.

There are probably four kinds of proteid present in the secretion from diseased prostates; serum albumin, serum globulin, nucleo-albumin, and deuto-albumose. Acetic acid will precipitate the nucleo-albumin and give a white ring at the zone of contact if used in a layer test. If mixed with the urine a white precipitate collects at the bottom when it is allowed to stand for several hours. Soon after its being passed flocculent masses of nucleo-albumin are seen to form about the center of the glass of urine.

The proportion of serum albumin and nucleo-albumin varies with the condition in the prostate; abscess cavities furnishing large amounts of serum albumin, while catarrhal inflammation of the lining membrane of its ducts and follicles give an excess of albumose and nucleo-albumin. Between these extremes will be found many grades of inflammation with a varying ratio and combination of the proteid. Nucleo-albumin is derived from the disintegrating cells and is very similar to mucin.

The presence of spermatozoa in albuminous urine should always suggest the possibility of the inflamed prostate or seminal vesicles being the source of the proteid. From considerable study of this subject I have reached the conclusion that spermatorrhoea, instead of being a neurosis or due to a patulousness of the ducts of the vesicles, as is claimed by most authorities, is really nothing more nor less than a low-grade inflammation of the mucous membrane of the seminal vesicles. The increased secretion formed by the inflamed surface distends the cavities and finally by pressure or overflow, the fluid is discharged into the bladder or at the meatus, carrying with it spermatozoa. The inflammation that reaches the vesicle is of exactly the same character as that which causes an urethral discharge or a prostatorrhoea. I see no reason for believing that when this inflammation attacks the mucous lining of the vesicles or the ampullations of the vas deferens, it should act differently and cease to produce an increase in the secretion. After the production of a vesicle full of fluid it does not

¹ Sahli; "Diagnostic Methods," 1905.

seem difficult to imagine that the expression of this secretion would take with it some of the spermatozoa. Why should we claim that spermatorrhoea is due to a dilatation or flabbiness of the seminal ducts any more than that a discharge from the urethra is due to a dilatation of the meatus or that a secretion from the prostate is due to the large caliber of its ducts? The causes of spermatorrhoea are exactly the same as those that produce prostatorrhoea and we all agree that this is an inflammation of the prostate.

In speaking of spermatorrhoea I mean only those cases in which spermatozoa can be demonstrated, with the microscope, in the discharge or urine, and not the patients in whom spermaphobia is an obsession and who believe every drop of clear mucous to be semen.

Many times the insidious onset of this inflammation makes the subjective symptoms and history of chronic prostatitis or vesiculitis worthless in the diagnosis.

To obtain the secretion from the prostate and vesicles separately the patient is requested to present himself with a full bladder, about three-fourths of the urine is voided, washing out the urethra. After this the prostate is thoroughly massaged leaving the vesicles untouched, its condition is shown by the remainder of urine which is now passed. The urethra and bladder are irrigated with a boric acid or normal salt solution, the vesicles are massaged and the fluid voided will show by its contents their condition. (An *excess* of proteid and pus cells if they are inflamed.)

I have seen several patients with a mild chronic vesiculitis in whom the amount of seminal fluid was too small to appear at the meatus or leak back into the bladder, but could be easily obtained by pressure on the lower part of the vesicles. The inflammation was apparent from the large amount of albumin, albuminose and pus cells present in the secretion swarming with spermatozoa. This condition a little more advanced results in a true spermatorrhoea.

In my former paper on this subject the periodic increase in the prostatic secretion every ten to thirty days, that was observed in patients with chronic prostatitis, led me to suggest the similarity between this condition and menstruation in women, as I consider the prostate the analogue of the uterus. In the discus-

sion before the Atlanta Medical Society one of the members thought my analogy "farfetched" as he believes the veru montanum and the womb analogous. My reasons for believing otherwise is that: there is too great disparity in the size of the veru montanum and the uterus and I do not see the reason for selecting this small central portion of the prostate and considering it the analogue of a much larger organ, the uterus, whose structure corresponds more accurately with the tissue of the prostate proper, both being composed largely of muscular and glandular tissue.

The prostate is the only organ situated between the bladder and the rectum in the male which could be considered the counterpart of the uterus. The course of the canals leading from the ovary to the womb, which corresponds to the vas deferens connecting the testicle with the prostate, apparently offers further confirmation of the view of the analogy.

CONCLUSIONS.

The presence of albumin and albumose in the urine voided after massage of the prostate, when that passed before is normal, is as reliable in the diagnosis of prostatitis, or an abscess draining into the urethra, as renal albumin is in the diagnosis of kidney disease. This was constantly found in twenty-five patients with inflamed prostates. In two of these, with acute prostatitis, the first urine for a few days, showed as much as 1 per cent. of proteid, without evidence of renal disease at *any* time. The test was negative in fifteen patients with healthy prostates and vesicles.

The recognition of this prostatic and vesicular proteid affords a very simple method of making a positive diagnosis of prostatitis and seminal vesiculitis (when in excess) and is available in mild obscure cases whether a microscope be at hand or not.

An overflow of the secretion from the prostate or vesicles may contaminate the urine and mislead one as to the significance of the proteid present. In doubtful cases it should be eliminated by obtaining urine for examination ten or fifteen minutes after massage of the prostate and vesicles and a thorough irrigation of the urethra and the bladder, or if this fails by the history,

the absence of symptoms of nephritis and casts, and if necessary by ureteral catheterization. An increase in the amount of the proteid after massage should always suggest the prostate or the vesicles as the source.

Owing to the alkalinity of the prostatic secretion and to the fact that a large part of the proteid is deuterio-albumose, which is not precipitated by boiling, the heat test as ordinarily applied will not be satisfactory as many times no cloudiness will appear in the part of the urine boiled. Picric and citric acid will, however, produce a cloudiness or a precipitate when the urine is cool. This will disappear when heated if due to albumose. If the urine be added drop by drop to a test tube of boiling water the proteid can be readily detected by the little clouds formed as it mixes with the water.

Robert's solution, as modified by Boston, containing one part of nitric acid to ten parts of a saturated solution of magnesium sulphate applied as a layer test, will demonstrate still smaller quantities and is the method upon which I rely in routine examinations.

A study of these secretions has led me to the conclusion that spermatorrhoea, instead of being a neurosis or due to a patulousness of the seminal ducts, as most authorities claim, is really caused by a low-grade inflammation of the seminal vesicles and the ampullations of the vas deferens, which should be borne in mind in the treatment of these conditions. The inflammation causes an increase in the secretion which mechanically washes out the spermatozoa.

OXALURIA AS A CAUSE OF PROSTATIC AND URETHRAL DISTURBANCE.*

By GEORGE KNOWLES SWINBURNE, M. D., New York.

DURING the past two years I have been so struck by the large number of patients in my practice as well as of those who have come to consult me after having received prolonged treatment at the hands of others without benefit, in whom a condition of oxaluria was either the sole cause of prostatic or urethral disturbance, or was the secondary cause of the continuance of the original trouble and had been overlooked, or if not overlooked, then ignored, that I have ventured to bring the subject to the notice of this Society.

Believing that this subject had not received the attention that it deserved, I made an examination of the latest text books at my command and found that this was so; I omitted, however, to make any search of recent literature, or I should have remembered an admirable paper read by Dr. Bransford Lewis of St. Louis, before the American Association of G. U. Surgeons in Washington on May 6, 1897, and published in the *Journal of Genito-Urinary and Cutaneous Diseases* in July, 1897, in which his findings are exactly similar to my own.

I suppose that every practitioner knows—theoretically at least—that a non-specific urethritis may be caused by oxaluria and yet, a physician whose practice is largely genito-urinary, wrote me a few years ago that for some two or three weeks he had been troubled by a muco-purulent discharge with burning on urination; he had at once recognized that it was not a gonorrhoea and furthermore, he had never had an attack, nor had there been an exposure. He wrote that he had been taking alkalies, but had obtained no relief. I wrote back asking him to make a microscopic examination of the urinary sediment; he answered that all he could find were a few crystals of oxalate of lime. I ad-

* Read at the annual meeting of the American Urological Association, Boston, June 5, 1906.

vised him then to try nitro-hydrochloric acid and shortly after received another letter thanking me for the advice and saying that he himself had quickly recovered from an unpleasant condition, and that curiously had recently been consulted by a former patient whom he had some time before treated for a gonorrhoea, whose condition was similar to his own recent trouble and that an examination of the urine disclosed oxalate of lime, and he had been able to clear up his condition quickly by administering the same prescription.

Late one evening a physician, about thirty-two years old, came to ask me if I could suggest anything to relieve his condition: for the past three months he had been having repeated nocturnal emissions which had been occurring with such frequency, lately every night, and even more frequently, that it had "gotten on his nerves." He was married, a college graduate, an unusually intelligent man and a very hard worker. He had never been given to sexual excess, had never had any venereal disease, and such a condition had never happened to him before. At times he had suffered a good deal from pruritus ani. Local examination showed nothing abnormal except a slight hyperaesthesia of the posterior urethra on passage of the Thompson searcher. The urine was perfectly clear and contained neither albumin nor sugar, but I omitted at the time to make a microscopic examination. Appetite was not especially good and there was a slight tendency to constipation. I told him I thought his condition came from the condition of the alimentary tract and that his trouble would in my opinion clear if he attended to that. About two weeks later I met him and he told me that his indisposition had cleared entirely in a few days.

Not having examined the urine microscopically, I should not relate this case, were it not for its resemblance to the following case:

A. B., twenty-eight years old, an accountant, unmarried, had for six months previous to consulting me, been troubled by nocturnal emissions which had so increased in frequency in the last six weeks that he determined to have his condition examined into. He was a college graduate, had always been fond of athletic sports, but his business had recently kept him confined and he had little time for exercise, never had any venereal disease

and had always been continent, and at the present time was engaged to be married. There had been no sexual excitement of any kind. An examination of his urine showed numerous oxalate of lime crystals, and a single dose of calomel taken at night, followed by salts the following morning, together with dil. nitrohydrochloric acid taken after meals for a week or so, cleared up his case completely.

D. K., twenty-eight years old, a farmer, a large powerfully-built man with a clear ruddy complexion, the picture of good health, came in the winter, two years ago, complaining of sexual weakness. As a boy had masturbated to some extent and later on coming to the city to live had had intercourse several times, but had escaped venereal disease. While here, had consulted an advertising quack who had passed sounds for the supposed sexual weakness. He left the city after having lived here for a year or so, and returned to farm life. But he had always regarded himself as sexually weak and it troubled him that slight provocation would cause the exudation of a glairy mucous discharge. Examination showed some prostatic congestion, but I advised him to do his best to make a success of farming and not let his mind run on sexual matters, and get himself in a position to get married. Early this past winter he came again and said that at times his condition had become much worse, he could not drive, sitting in seat of his farm wagon without having, as he expressed it, seminal losses, which were weakening him, they being of daily recurrence, and he seriously asked if he could not go to a hospital and have his testes removed, his present condition being unbearable. I made as careful an examination of him as possible and found that he had a real condition of prostatitis. Through the urethroscope the deep urethra appeared much congested, but the urine was loaded with oxalate of lime crystals. I gave a single dose of calomel and sodium bicarbonate aa gr. X, at night, followed by sulphate of magnesia the following morning and nitrohydrochloric acid after meals. When he returned two weeks later, his condition had improved markedly; he could sit on the seat of his farm wagon without being obliged to sit forward on the very edge of the seat. Also his mental attitude had changed. I then treated his prostate by massage, and made a few applications, swabbing the deep urethra through the urethro-

scope with 10% Ag No. 3 solution, and tried to show him how to take care of himself in the future.

A. G., fifty-five years old, a baker, came to the dispensary, complaining of burning urination and of frequency, both day and night. The urine was clear. He completely emptied the bladder, so there was no residual urine. The urine showed numerous crystals of oxalate of lime. His prostate was normal. He had a heavily coated tongue and was of a constipated habit. He was under treatment for several weeks and finally seemed to do best on one of the Dispensary formulae of dil. nitrohydrochloric acid and essence of pepsin. The crystals finally left the urine and he felt perfectly well again.

W. T., tall and spare, but good build, forty-five years old, for two months had been having a muco-purulent discharge, had had several attacks of gonorrhoea, but not for many years. He first noticed the present trouble a few days after an intercourse, consulted a prominent physician in Toronto where he was living at the time, who without making any examination told him he had a gonorrhoea and prescribed Santal oil. The discharge remained the same, neither diminished nor increased, and on coming to New York to live went to a physician near his home who treated him with irrigations of permanganate of potassium. His condition remained unchanged and he was referred to me for treatment. I found his prostate soft and boggy and expressed considerable material on massage. No gonococci could be found. The bladder urine was clear. Under massage and irrigation with argyrol the condition of the prostate improved, but he complained of a condition that was annoying him exceedingly and consisted of attacks of heat and pain, deep seated in the canal. They came on independently of urination, would last several minutes and then pass off, and in their manner of onset resembled attacks of pruritus. The deep urethra was treated through the urethroscope. In the beginning the urethra was so congested that it bled freely after the insertion of the urethroscope, which treatment by the way I limit to weekly applications. After each application there was less bleeding, till after four to six sittings under such treatment the urethra had returned to a normal condition. But he still complained of these attacks of heat and pain and was becoming neurasthenic. The muco-purulent discharge had prac-

tically ceased. I then for the first time made a microscopic examination of the urine and found a marked condition of oxaluria. The calomel and saline were followed by the nitrohydrochloric acid. I saw him once after that, when he stated he had experienced considerable relief and was going away to the seashore. I have not seen him since.

I will relate but one more case. A. M., thirty-five, came to the Dispensary about five years ago for a chronic gonorrhoea; had been laid up in the hospital with epididymitis. He came for about three months, and I remembered the case well, because it was one of the first on which I had used my posterior urethroscope and discovered a large swelling with a granulating surface about the middle of the verumontanum; on withdrawing the instrument it had curetted the surface and the small tumor was found in the window of the instrument, followed by some little bleeding. At that time several applications were made and then the patient disappeared. I did not see him again till this past winter, when he came to see if he could be cured of a condition that had persisted since he had left the Dispensary. This consisted of attacks coming on independently of urination of a stabbing pain in the region of the prostate and deep urethra, which would last from a few moments to over an hour, after which he felt weak. Sometimes he would go for several weeks without an attack, and sometimes they were quite frequent; when severe and prolonged, he would have only one attack during the day, and sometimes, when milder, they might persist throughout the day. At the time he left the Dispensary, his urine was very cloudy, but now was perfectly clear except for a long mucous shred which at first floated and then gradually sank to the bottom of the first glass. The prostate, which before had been large and somewhat nodular (I remember I feared at one time the possibility of tuberculosis), was now perfectly normal and regular on palpation, no material being expressed. The deep urethra was congested. The urine showed an oxaluria. The treatment has been largely directed toward the alimentary tract. He has been under observation during the better part of six months. At times he has no trouble whatever and then an attack will come on, but they have diminished in severity. When he feels well, there is no oxaluria and after such an attack I have always found it present.

Now, in the past year I have had twenty-six cases of oxaluria, presenting a variety of symptoms such as I have stated, but the greater number of these cases show the same general set of symptoms. There is a history of a previous gonorrhoea of a recent or remote date; ever since the attack there has been a persistent burning pain in the canal, usually at the end of urination, sometimes quite sharp and of a nagging character. Some have been the victims of every sort of application their physicians could think of and have been their despair. There may or may not be present a muco-purulent discharge; generally they show nothing but a few shreds in the urine. Such patients have been told it was their imagination, that they were cured. They all have oxaluria; some have yielded readily, others persist with their symptoms and their oxaluria in varying degree, sometimes better and sometimes worse.

I think I cannot better conclude than by quoting the summing up of Dr. Lewis's article:

"(1). Both oxalic and uric acid may appear in the urine, either in a physiological or a pathological manner.

"(2). When pathological, they may exert certain injurious effects on the genito-urinary organs.

"(3). These effects may be either the inciting of disease where there has been previous health, or they may act by rendering more serious and resistant to ordinary methods of treatment other inflammations and disorders (gonorrhoeal, etc.), of those organs.

"(4). When either the oxalic or uric acid element is acting injuriously in the ways mentioned, systemic treatment (dietary, medicinal and hygienic) is demanded, and may even take precedence over the local measures that are usually considered sufficient in such inflammations or disorders."

This, however, is not all. It seems to me that these cases are worthy of study and are cases for the general practitioner. Some of these cases are apt to develop renal calculus, and I think that a previous gonorrhoea may predispose to this condition, as also may an invasion of the urinary tract by the colon bacillus. They are due to faulty metabolism.

DISCUSSION.

Dr. E. L. KEYES, JR., New York: It seems to me that in many of these instances of general debility or neurotic habit and irritability of the posterior urethra showing itself in various ways, the two conditions are due to a common cause rather than one due to the other. I think the danger in most of these cases is in overdoing local treatment and not turning the man out to grass sooner.

Dr. SWINBURNE (Closing). There is nothing to add. Some of these cases, I might say most of them, have been rather difficult, but I hoped to get some light on the best methods of treatment. Of course the treatment must be in a measure, systemic, and I agree with one thing Dr. Keyes said, which was, that instead of the oxaluria causing some of these symptoms, it as well as the urinary and prostatic symptoms may both be due to an underlying cause.

CHRONIC CATARRHAL NEPHRITIS.¹

By I. N. DANFORTH, A. M., M. D., Chicago.

IN the month of May, 1885, I read a paper before the Illinois State Medical Society, entitled "Simple Renal Catarrh," which commenced as follows: "More than ten years ago, my attention was attracted to a peculiar and quite common form of renal irritation, which receives no distinct recognition in our text books." It is therefore at the present time more than thirty years since I began to observe the condition which I then called "Simple Renal Catarrh," but which I now call Catarrhal Nephritis, because from long observation and experience, I am satisfied that it merits the dignity of a name of its own, and a place of its own in our catalogue of diseases. What then is meant by "Catarrhal Nephritis"? As I stated, twenty years ago, "it is essentially a catarrhal inflammation, or an inflammatory process of very low degree, which has its seat mainly in the renal tubules." I will now qualify that statement by saying that its pathologic consequences are mainly manifested upon the epithelial cells of the renal tubules. It may commence in any portion of the tubuli uriniferi, from the capsule of Bowman to the papillary terminals of these tubules; yet my belief is that in the majority of cases, it has its origin in the convoluted portions of the tubes, because

¹ Read by title at the annual meeting of the American Urological Association, Boston, June 4-5, 1906.

the exciting causes are most commonly found in these tubules, as I shall presently show. In exceptional cases, as in neglected or ill-treated instances of bladder infection, the maladroit use of ureteral catheters or instruments for bladder exploration, the cause of renal catarrh may come from below and travel upward to the renal parenchyma, as true instances of so-called "upward infection."

The changes in the renal cells are quite characteristic. They become swollen and cloudy, and somewhat opaque; in other words, they manifest the usual appearances of cloudy swelling, and they secrete an abnormal amount of thick glassy mucus, which renders the urine more or less turbid, according as the mucus is greater or less in quantity. The whole kidney is generally hyperemic, sometimes to a very slight degree, sometimes very markedly so. The organ generally presents a swollen appearance, so that the capsule seems drawn very tight, and if the latter is incised for an inch or two, on the convex border, the kidney structure will bulge through the opening, as though the organ had outgrown its capsule. If microscopic sections of the kidney are made, they will show cloudy, swollen epithelial cells, crystals of urinary salts, and strings of thick sticky mucus—provided, of course, the sections are made from kidneys removed from the body very soon after death, and are examined at once, without special staining, or other preparation.

SYMPTOMS. Catarrhal Nephritis has no distinctive subjective symptoms. If associated with lithuria, phosphuria or oxaluria, the characteristic symptoms of either of these conditions will suggest the presence of renal catarrh, and of course the necessary investigation will follow. Or, if there is a history of chronic bladder or vaginal infection, it is probable that the kidneys will be implicated. Such cases as these present tangible and definite causes, and one has no difficulty in arriving at a reasonable conclusion by a process of "diagnostic induction." But there remains a large group of cases which seem to arise without any appreciable cause, and which are likely to elude a painstaking diagnostician, unless he is alive to the fact that catarrhal nephritis is a very common malady, and may be present when least expected. Whenever a case presents itself with impaired digestion, a coated tongue, foul breath, fickle appetite, flatulence, con-

stipation and a general demoralization of the gastro-intestinal tract, it may safely and easily be predicated that imperfect elimination, and consequent toxemia are important and probably primary factors in the causation of the symptoms noted. Of course the next question will be what is responsible for the imperfect elimination, and generally it will be laid to the liver, and I may add, not without reason. But it is likewise true that in a great many cases, the liver is not the only, nor yet the chief sinner; but the renal function is imperfect and faulty, and an examination of the urine will reveal the presence of catarrhal nephritis. In other words, the existence of the symptom complex which I have noted, should suggest the possibility of renal failure, and an examination of the urine. Sometimes patients will complain of backache, which will be called lumbago; or of frequent urination, which is likely to be attributed to "catarrh of the bladder," and very properly, because the bladder is provoked and irritated by the presence of morbid urine, sent down by morbid kidneys. The patient has no temperature, does not lose flesh, is not disabled from business, yet is languid, and lacks his accustomed vigor, albeit there are many cases without any symptoms, local or otherwise, of sufficient positiveness to attract the attention of patient or physician, yet both patient and physician are aware that the health of the former is not quite perfect.

But an examination of the urine will furnish evidence sufficient for the establishment of a positive diagnosis in practically every case, provided a proper and careful examination is made. I have long abandoned the practice of telling my patients to bring me a specimen from the entire quantity passed in twenty-four hours, because such specimens are likely to become mixed with dust from sweepings or clothes brushings, or with some other person's urine, or with sputum, or they are likely to decompose in hot weather, or get too chilled in cold weather, and any or either of these accidents impair the reliability of the specimen. Let the patient save a twenty-four hour specimen, and report the quantity, but for chemical and microscopic examinations, something different is desirable. I am accustomed to tell patients to procure from the druggist two four-ounce bottles, be sure they are freshly washed, and freshly corked with clean, new corks; then to fill one of these bottles with the urine passed on going to

bed, and the other with the urine passed on rising the following morning, both specimens to be brought to me the same forenoon. If these two specimens are mixed in equal quantities, the result will be a specimen which will fairly represent the average daily work of the kidneys. And what shall we find, if the case be one of catarrhal nephritis? As regards quantity, it is likely to be markedly in excess, or markedly deficient; in exceptional cases, normal in amount. The color may be light or dark, according as the quantity is large or small; the reaction is generally acid in fresh specimens, sometimes sharply, sometimes feebly so; in specimens not strictly fresh, the reaction is likely to be alkaline; the specific gravity may be as low as 1005, or as high as 1030, and this is closely related to the volume or amount of urine. The specimens are usually turbid or cloudy, but may be clear and beset with crystals which sparkle when the urine is held between the eye and a strong light, solar or artificial. When the urine stands for any length of time, a thick deposit falls to the bottom of the bottle, which is composed mainly of a thick, clear, glassy, transparent mucus, quite unlike that of vesical catarrh; in fact, I think this peculiarly glassy mucus may be regarded as characteristic of renal catarrh. Albumen may be present in small amount—generally only “a trace,” if any; or it may be absent; or it may be present at one time and absent at another; or again, it may be present all the time in one case, and absent all the time in another. In most cases, it will be present in a barely appreciable quantity, when the patient is actively at work, and absent during his hours of absolute rest. No general rule can be laid down; each case must be classed by itself, but almost every case has slight albuminuria at some period of its course. It seems scarcely necessary to say that the testing must be done with delicacy and skill, if reliable results are to be expected. The microscope will show plenty of epithelial cells from the renal tubuli and pelvis, and some patches of squamous cells from the bladder; also many leucocytes, and probably various forms of crystals of uric acid and other saline deposits, as sodium urate or calcium oxalate, or if the urine is alkaline, mixed phosphates. There will be present the so-called “cylindroid casts,” which, I think, may be regarded as characteristic of renal catarrh. The name “cylindroid” is not a happy one, because it means nothing. The casts in question are long,

wavy, rather irregular strings of mucus, or more correctly mucin, which have been formed in the renal tubules, and washed or floated away by the stream of urine accumulating behind them. They are more or less perfect casts of the tubes in which they were formed; hence they vary much in size, form, length and general appearance. They are structureless and have a somewhat high refractive power; hence they are often difficult to find, and may escape notice altogether, unless the observer is very familiar with their appearance. It is a good plan to add a couple of drops of Loeffler's alkaline blue to a suspected specimen of urine, a few moments before centrifuging, so as to stain the casts and other organic bodies. These casts or "cylindroids" are the product of the catarrhal process; they are the fruit of a morbid secretion by the epithelia of the renal tubules; but they must not be regarded as the product of an exudation directly from the blood vessels, like the fibrinous casts of parenchymatous and interstitial nephritis. A few blood-globules may be present, but it would be a temporary incident, and not a legitimate event, if the case is one of uncomplicated catarrhal nephritis. Colon bacilli are almost always present; gonococci are liable to be present, if the case is one of upward infection, and of course the ordinary pus germs are liable to appear at any time.

The causes of catarrhal nephritis are mainly toxic or septic. Under the head of toxic causes, I would include uric acid and its allies, calcium oxalate, the phosphatic compounds, and, rarely cystinuria; including, of course, the various complex combinations of these bodies, which are constantly taking place either in the blood, or the renal parenchyma. When the saline elements of the urine are very much in excess of the normal amount, they are pretty sure to be precipitated in the renal tubes, in the form of crystals or granules or both, and these particles, with their sharp angles or rough surfaces, are certain to prove seriously irritating to the tubules and particularly to their delicate epithelia. The first result will be the development of a catarrhal inflammation in the tubes so invaded, and the subsequent appearance of the symptoms and phenomena already described. These cases find their counterpart in the numerous instances of catarrhal bronchitis, produced by inhalations of dust particles, and their irritating effects on the bronchial mucous membrane. The most frequent and potent of

the toxic causes of catarrhal nephritis, is unquestionably uric acid, which is so prone to precipitate along the course of the renal tubes, and form little irritating masses, which promptly provoke a response in the shape of renal catarrh. As this precipitation almost always occurs in the convoluted tubes of the kidney, simply because these tubes are chiefly the functional portions of the organ, it follows that toxic catarrhal nephritis is most likely to have its origin in the so-called "labyrinth" of the kidney. Of course the urates, phosphates, and oxalates are equally capable of doing similar mischief, but they are, at least, not so frequently detected in the very act, as is uric acid. But they are certainly frequent and efficient accomplices in the production of renal catarrh, and other lesions of the kidney, after uric acid has paved the way.

The septic causes of renal catarrh are chiefly instances of "upward infection," in which septic germs travel upward from the bladder. Among these germs, the gonococcus undoubtedly holds first rank, although the various pus germs are perhaps no less certain as regards results, but they are much slower in their migration, much less serious as to consequences, and much more easily eradicated than the malevolent gonococcus. In females, examples of upward infection and consequent catarrhal nephritis are exceedingly common, the infection being communicated from the vagina to the bladder, and thence along the ureter to the kidney. I have seen a great many cases, in which the history pointed unmistakably to the chain of events just described; a gonorrheal infection being followed in due time by an infected bladder, and then by infected kidneys. Of course many of these cases develop into suppurative pyelitis or pyelo-nephritis, but in quite a proportion of them, the infection of the kidney is of a very mild type, and may be arrested in the catarrhal stage, if detected in season. But not all cases of septic catarrhal nephritis are due to upward infection. In fact, abundant clinical experience has proven that infection of the kidney may be communicated through the blood, from any portion of the body. It is not at all uncommon as a result of pneumonia, severe attacks of typhoid fever, diphtheria, and violent attacks of the eruptive fevers. I have seen many cases of renal catarrh occur during or following severe attacks of the epidemic influenza, which goes by the name of "la grippe." In fact, any long severe illness, which is of itself of a toxic or

septic nature, may provoke an attack of renal catarrh as one of its sequelæ. In such cases, however, it is not always possible to decide whether they should be regarded as septic or toxic; nor is it a question of any great practical importance, from a clinical standpoint. There yet remains a group of cases, neither very large nor very frequent, for which no causes can be assigned. They are generally said to result from cold, exposure, stormy weather, overwork, intemperance, etc., and it is probable that, once in a while at least, one or more of these conjectures may hit the nail on the head.

The prognosis of catarrhal nephritis ought always to be favorable, and so it would be, if an early and correct diagnosis could be made. But unfortunately we physicians depend too much upon "symptoms" and as I have already said, the disease under consideration has no symptoms that are positive and characteristic, except those derived from examinations of the urine, and such examinations are oftener the exception than the rule. In clinical experience, it will be found that a considerable group of very mild cases develop, run their course of a few days or weeks, and get well spontaneously, without recognition or treatment. I make this statement as a result of my own observations of many cases, during the past twenty years. Another group of cases of greater severity, but which are fortunate enough to be diagnosed early and treated wisely, make good and perfect recoveries, after a period varying from one to three months. Still another group of cases, which are of unusual severity from the start, or do not happen to be promptly recognized, and are not judiciously treated, will eventuate in true Bright's disease, or pyonephrosis, or renal calculus, or some combination or complication of these various lesions, thus transforming a very simple and easily-cured hyperplasia of the renal epithelia, into a very grave and possibly incurable disease, which extends its ravages to the whole kidney. Of course the resources of surgery are capable of reaching and curing many of the cases indicated, but an early diagnosis in every case of catarrhal nephritis, would, in my judgment, reduce the operations upon the kidney very materially.

In view of the astonishing prevalence of therapeutic agnosticism at the present time, one almost hesitates to say anything about the employment of therapeutic measures, lest he be deemed

"old-fashioned" and "out of date." Yet one cannot utterly cast aside the cumulative teachings of experience, common sense and science, even at the somewhat dogmatic dictates of "modern medicine." There is no better field for the exercise of rational therapeutics, than in the treatment of catarrhal nephritis, and its importance, considered from the standpoint of "preventive medicine," can hardly be overestimated. It is mainly a question of the removal of the causes, after which the disease gets well of itself. In all forms of renal catarrh, the first thing in order is a proper regulation of the diet. Proteids must be cut down to a limited amount, once a day, although I have long ceased to forbid flesh diet altogether, because a certain amount of nitrogenous food seems necessary for perfect nutrition. Milk, cereals of all kinds, fruits and vegetables are allowed in reasonable amount. Tea and coffee are permitted sparingly. All forms of alcoholic stimulants are forbidden; tobacco is generally interdicted, but an old and inveterate smoker is allowed two mild cigars a day. The patient is admonished to masticate his food thoroughly, or "eat slowly," and this I regard as of no trifling importance, and I generally accentuate my advice by reminding the patient that he is not provided with a gizzard, like a chicken, to grind his food after he has swallowed it. If his teeth are not capable of efficient mastication, he is referred to his dentist. Not long ago it was the fashion among medical men to direct their patients with renal lesions of any kind, to drink "all the water they could," and quite too many of them tried to obey. At the various watering places it got to be a matter of emulation among visitors, to see who could drink the greatest quantity of water. I have seen many cases of nephritis of various forms, but especially catarrhal nephritis, which I believed to be directly due to the water-logged condition of the kidneys, consequent upon unreasoning devotion to the water-drinking fad. A somewhat liberal use of water—if it is pure water—is unquestionably beneficial in all inflammatory lesions of the kidneys, but when it is pushed to the extreme of overloading the blood vessels, and forcing the kidneys to act more like safety valves than like eliminating organs, it is time to call a halt. Violent exercise, like "strenuous" athletics, should be forbidden, but plenty of mild exercise, out of doors, is beneficial. Frequent tepid salt baths,

followed by vigorous body friction, will be helpful. As to medicines, if we are dealing with a case of uric acid poisoning, the administration of the potassium, sodium or lithium salts (citrate or carbonates are the best), in doses of ten to thirty grains, four times a day and always when the stomach is empty, will generally bring about satisfactory results. The remedy should always be given in a large glass of water, and if the water is quite warm, it is all the better. Many cases are benefited by sodium salicylate or aspirin, and a combination of sodium salicylate with potassium carbonate, in doses of ten grains of the former to twenty grains of the latter, three or four times a day speedily benefits many cases. Nearly every case of uric acid poisoning will yield to combinations of the salts of potassium sodium and lithium, but it is frequently necessary to use them for considerable periods of time, and patients with a pronounced uric acid diathesis, need a repetition of the treatment at longer or shorter intervals.

The condition known as oxaluria, or the oxalic acid diathesis (first described by Donné in 1838), is frequently associated with lithemia, and is to a considerable extent, at least, dependent upon the same causes. Its chief interest, for present purposes, lies in the great liability of the sharp-angled crystals to deposit in the renal tubules, and start a catarrhal process by mechanical irritation. The presence of oxaluria generally depends upon impaired digestion, indicated by the symptoms of "nervous dyspepsia." In addition to, or in modification of the treatment for lithemia, the patient usually needs a few doses of calomel, followed by strychnine, nux vomica, vegetable bitters or pepsin, such selections or combinations being made as are indicated by the particular case under treatment.

Phosphatic deposits in the urine may be either alkaline (sodium and potassium), or earthy (calcium and magnesium). (In decomposed urine, of course, the ammonio-magnesium or triple phosphate may be found, but that does not concern us in this connection.) The common alkaline and earthy phosphates are very frequent in dyspeptics, neurasthenics, victims of hysteria and other "functional" nervous affections, and all the wasting diseases, and the indications for treatment must be deduced from the underlying pathology of the case in hand. Patients with phosphaturia are frequently overworked business men, clergy-

men, lawyers and the like, and they are very numerous in these days of the "strenuous life." Very many of them have renal catarrh as an accompaniment or complication of the phosphaturia. A few weeks of absolute rest and recreation is all that many such patients need, but unfortunately it is just what most of them cannot have. We must therefore do the best we can for them, just as we find them. Faulty habits as to eating and drinking should be corrected; the bowels should be unloaded and kept thoroughly evacuated; the functions of the skin as an eliminating organ must be attended to, and the patient ought to be advised again and again as to the importance of daily, but moderate exercise in the open air. As to medicines, digestives and tonics addressed to the nervous system, will cover the ground. The mineral acids, especially the phosphoric, strychnine or nux vomica, and the vegetable bitters, like gentian, will be found useful. Cod-liver oil, the malt preparations, and the preparations of organic iron will also find their respective places in cases attended with anemia or "wasting." But, of course, these medicines must be regarded only as adjuncts to proper diet, correct habits and modes of life, including, so far as possible, the all-important let up from business and professional cares and worries.

In treating septic catarrhal nephritis, it is first necessary to determine what form or forms of sepsis we are dealing with, and next to ascertain its or their sources. Most cases will be examples of "upward infection," the septic germs making their way upward from the bladder, and in females many cases may be traced to a vaginal discharge, due to endometritis, which in turn is due to unhealed cervical lacerations. In all septic cases of renal catarrh, the cause must be hunted down and removed, else medical treatment will be little else than palliative. Unhealed cervical or perineal lacerations, hemorrhoids, anal fistulae, rectal ulcers, and all such sources of pus germs, must be explored and remedied, before any treatment addressed to the urinary tract will be of much value. In males, a chronic balanitis due to filthy habits or phimosis, a stricture which gives little or no discomfort to the patient, a prostatorrhea or cystitis, of which the patient may be unaware, or the presence of a few venerable gonococci in the urethral lacunae, and which now and then renew their youth and vigor, or some rectal lesion, slight in itself, yet sufficient to en-

courage the growth of septic germs; any one of these, as well as various other sources of infection, may install and perpetuate a renal catarrh, which will surely become a grave renal lesion, if not arrested in the catarrhal stage. Therefore, I repeat, seek out and get rid of the sources of infection, after which the infected kidneys may be treated with large prospects of success. The rules as to diet, habits, etc., already enunciated, apply here without modification or exception. The particular medical treatment of septic catarrhal nephritis, reduces itself to the persistent employment of any one of several remedies, and the selection must be left to the judgment of the physician, and his views of the case in hand. Urotropin, cystogen, aminoform, boric acid, benzoic acid, salol and benzosol are each and all very useful remedies in catarrhal nephritis, if there is a septic factor in the case. The one selected should be given in 5 grain doses, along with a glass of hot water, at least half an hour before each meal, and at bedtime, so that the remedy may, so far as possible, escape admixture with the food, and the effects of gastric digestion, and may enter the blood and reach its destination as rapidly as possible. Of course this is rather a finespun theory; yet I am sure that I get more prompt and positive effects from remedies destined to modify the renal apparatus, if given in this way, hence I insist upon its importance. In very obstinate cases, with profuse discharge of stringy mucus, I have derived great help from creosote, or Canada balsam, or capaiba, or sandal oil, given persistently, in doses not exceeding 5 minims, four times daily, freely diluted. There are plenty of remedies besides those mentioned, which are equally valuable, but it is better to be thoroughly acquainted with a few remedies, than to half know a larger number. The cure of any one of the chronic renal diseases—if they are curable at all—is not a question of polypharmacy, but rather a matter of a few remedies, wisely but persistently administered, and, at the same time the enforcement of proper regulations as to diet, dress, and all other matters, which promote health.